

Does being on HIV Antiretroviral therapy increase the risk of syphilis? An analysis of a large national cohort of MSM living with HIV in England 2009-2016

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Key messages

A resurgence in syphilis among gay, bisexual and other men who have sex with men (MSM) has been detected in England.

Increases in high risk sexual behaviour, such as chemsex among MSM living with HIV in England is thought to be linked to the increased use of anti-retroviral therapy (ART) and is major factor in the increasing diagnoses of STIs.

There was no significant evidence of an increased risk of syphilis in MSM receiving ART.

Abstract

Objective: A resurgence in bacterial sexually transmitted infections (STIs), notably syphilis, among gay, bisexual and other men who have sex with men (MSM) has been detected in England. A Canadian modelling study postulated that anti-retroviral treatment (ART) may increase susceptibility to syphilis. We assess the association between ART and syphilis incidence in a comprehensive national cohort of MSM living with HIV in England.

Methods: National surveillance data were used to create a cohort of MSM attending for both HIV and STI care in England between 2009-2016. Survival analysis was used to calculate the incidence of infectious syphilis during periods on and off ART. Multivariable Poisson regression was used to assess the association between ART use and syphilis, after adjustment for potential confounders, including, as a proxy measure for high-risk behaviour, being diagnosed with >1 other STI prior to a syphilis diagnoses.

Results: 19,428 HIV diagnosed MSM contributed 112,960 person-years of follow-up from 2009-2016. The overall rate of syphilis was 78.0 cases per 1,000 person-years follow-up. Syphilis rates were higher among men receiving ART (36.8) compared to those not (28.4)

(absolute rate difference 4.7 cases per 1,000 person-years). Multivariable analysis showed no statistical association between receiving ART and syphilis. Increased risk of syphilis was found in MSM aged 25-34 (HR:1.89, 95% CI:1.43-2.51) and in those diagnosed with two other STIs (HR:5.83, 95% CI:5.37-6.32).

Conclusion: Whilst we observed a small increase in the rate of syphilis among those on ART, when adjusting for potential confounding factors, including a proxy measure for high-risk behaviour, there was no evidence of an increased risk of syphilis in MSM receiving ART. High-risk sexual behaviour markers were the main risk factors for syphilis and our results highlight the need for STI prevention interventions in MSM living with HIV to target these particularly high risk sexual networks.

Introduction

A resurgence in bacterial sexually transmitted infections (STIs) has been observed in England in recent years, especially among gay, bisexual and other men who have sex with men (MSM) [1]. Between 2012 to 2019 the number of syphilis diagnoses among MSM in England increased from 2,138 to 5,687 (increase of 166%)[2]. Increases in other bacterial STIs were also seen among this group, with chlamydia diagnoses increasing from 8,341 to 23,187 (increase of 178%) and diagnoses of gonorrhoea from 10,933 to 33,853 (increase of 210%).

Among MSM, HIV/STI co-infections, particularly syphilis, represent a significant public health problem [3]. A major factor in the increasing diagnoses of STIs among MSM living with HIV in England is thought to be changes in sexual behaviour and increased high-risk sexual behaviour which have been linked to the increased use of anti-retroviral therapy (ART). It has been suggested that there has been an increase in some high-risk behaviours such as chemsex (the use of drugs before or during planned sexual activity to sustain, enhance, disinhibit or facilitate the experience) [4-6] and a reduction in behaviours such as serosorting (selecting partners based on their HIV status), which is likely associated with both a reduction in the stigma towards HIV which is now often considered a chronic, manageable condition and the increased widespread use of ART.

Non-behavioural changes have also been suggested to explain the marked increase in syphilis over the last decade. More frequent monitoring of individuals with HIV may partially explain the elevated rates of STIs, particularly those who are asymptomatic [4]. Since 2014, UK national guidelines have recommended that all sexually active MSM test for STIs at least annually and those at high risk of STI acquisition, indicated by condomless sex with new partners and drug use, test after every episode of condomless sex [7]. A result of this, an increased emphasis on screening was observed through the number of sexual health screens among MSM which increased by 65% (149,909 to 248,154) between 2014 and 2018 [2, 6]. This increase may help to explain the increasing rates of STI diagnoses among this group. An alternative hypothesis for the recent increase in STIs is the emergence of *Treponema pallidum* (*T. pallidum*) strains with increased transmissibility [3], however adequate genomic data does not currently exist to support this hypothesis.

A recent Canadian modelling study by Rekart *et al* of HIV-1 and *T. pallidum* coinfection from 2005 and 2014 showed that both behavioural change and the use of ART substantially increased syphilis prevalence at baseline [8]. The authors concluded the behavioural impact of the use of ART could not fully explain the ongoing outbreak and that the immunological effects of ART may directly alter the host immune response to *T. pallidum*, resulting in increased susceptibility to syphilis.

To establish whether, using surveillance data, we also find a relationship between factors other than behavioural among those using ART and the incidence of syphilis in England as found by Rekart *et al* in Canada, in this study, we look for evidence to support this hypothesis by assessing the association between ART and syphilis incidence, in a national cohort of MSM living with HIV in England. Identifying any association between the incidence of syphilis and ART use that could be contributed to factors other than behavioural factors could provide us a better understanding of the syphilis epidemic among MSM living with HIV and indicate the need for further research into the biological feasibility of this association.

Methods

We performed a retrospective cohort analysis of all MSM receiving both HIV and STI care in England between 2009 and 2016 using HIV and STI surveillance data. To investigate the association between ART status and the incidence of syphilis we calculated the rates of syphilis (primary, secondary and early latent) in MSM living with HIV during periods on and off ART. Sensitivity analysis was carried out by including cases of primary syphilis only and as a comparator, the same methods were used to assess the rates of chlamydia and gonorrhoea on and off ART.

Data sources

Data on persons living with HIV were obtained from the HIV and AIDS Reporting System (HARS), a pseudonymised national cohort of all persons diagnosed with HIV and accessing specialist HIV care in the UK. Data, including ART status, are regularly updated at least annually by all service providers [9]. Data on STIs were obtained from the GUMCAD STI surveillance system, the national STI surveillance system in England [10]. GUMCAD records all attendances at all publicly commissioned sexual health clinics and collects information including STI testing and diagnosis details, patient registration information such as, demographic information including, ethnicity, country of birth, age, sexual orientation [9, 11]. Patient records are pseudonymised and can be linked within but not across clinics using clinic numbers that are unique to each individual.

Using a combination of clinical (clinic identification code, clinic site code, local authority of clinic and date of diagnoses) and demographic characteristics (gender, year of birth, ethnicity) we identified MSM living with HIV in HARS who also attended for STI care in GUMCAD.

Matching between the GUMCAD dataset to the HARS dataset was carried out for two groups of patients captured within the GUMCAD dataset; a) individuals who were reported as living with HIV in the GUMCAD dataset and b) individuals who were not reported as living with HIV in GUMCAD were matched. Data matching was carried out using a verified matching algorithm that was previously used to match tuberculosis and HIV data [12]. Only individuals who matched between both datasets were included in the study. A dataset was created containing individuals with diagnosed HIV matched to their full STI clinic history for analysis.

Study Population

The study population comprised MSM aged >15, living with diagnosed HIV and who had an episode of clinical care captured in both HARS and GUMCAD during the study period which ran from 2009 to 2016. Using the HIV diagnosis date reported in HARS we determined the initiation of follow up for each individual within the matched dataset. For men diagnosed with HIV before 1st January 2009, when the GUMCAD surveillance system was initiated, we considered the start of their follow-up time to be the 1st January 2009. For men diagnosed with HIV after the 1st January 2009 we took the start of their follow-up time to be the first recorded visit date in GUMCAD after their HIV diagnosis date. Individuals contributed person-years at risk from their entry into the cohort to their last attendance date reported in GUMCAD before December 2016, when follow up was censored.

Data analysis

Based on information reported to HARS, individuals were classified as either on or off ART treatment at each GUMCAD attendance. This was used to indicate ART status during each period between attendances reported in GUMCAD and was based on the most recently recorded ART status in HARS within one year prior to each GUMCAD attendance. CD4 count was categorised into <200, 200-349, 350-499 and >500 cells per mm³ and viral load was categorised into <50 (virally suppressed), 50-200 and >200 copies/ml. There was no evidence for co-linearity between CD4 count and viral load within the data. We included episodes of early syphilis (primary, secondary or early latent syphilis) but not late syphilis (late latent or tertiary), as reported in GUMCAD. For the purpose of these analyses, we considered episodes of chlamydia or gonorrhoea each as single infections irrespective of the anatomical site of infection.

For use as a proxy measure of high risk sexual behaviour, we calculated the number of other bacterial STIs (chlamydia, gonorrhoea or syphilis) each individual was diagnosed with during their time in the study period, an approach that has previously been validated as a proxy marker using GUMCAD data [13]. For example, when analysing rates of syphilis, we calculated the total number of chlamydia and/or gonorrhoea diagnoses (other bacterial STIs) that an individual had reported in GUMCAD prior to their syphilis diagnosis. We categorised these counts as none, one or two or more episodes of other bacterial STIs.

To investigate the impact of the use of ART on syphilis we calculated the crude incidence of syphilis per 1000 person-years. A multivariable random-effects Poisson model was fitted to assess associations with the risk of each STI after adjustment for the following confounders: age, ART status, viral load, CD4 count, previous other bacterial STI diagnoses and year of diagnoses to account for secular trends.

Ethical considerations

The study was approved by the London School of Hygiene & Tropical Medicine research ethics committee (Reference:13542). The Caldicott Panel at Public Health England provided oversight and approval for matching the HARS and GUMCAD data for this analysis. In its role providing infectious disease surveillance, Public Health England has approval to handle data obtained by GUMCAD and HARS under Regulation 3 of the Health Service (Control of Patient Information) Regulations 2002.

All data matching and statistical analyses were carried out using STATA 15 1.0.

Results:

Of the 10,030,027 unique individuals who were reported to GUMCAD between 2009 and 2016, 151,679 were living with HIV or reported as newly diagnosed with HIV at some stage during this period and 73.4% (111,253) were matched to HARS. An additional 7,176 matched individuals who were not reported as living with HIV GUMCAD but had a confirmed HIV diagnosis in HARS were also included. The resulting matched dataset provided a cohort of 118,429 individuals, of whom 19,428 were MSM living with HIV who had a recorded care visit for their HIV in either HARS or GUMCAD between 2009 to 2016. These men contributed 115,621 person-years of follow-up. The median years of follow up was 6.5 years per person (IQR:3.7-8.4).

Characteristics of the matched cohort of MSM living with HIV used in the analysis were compared to all MSM reported as living with HIV who are captured in the GUMCAD dataset to determine how representative the matched cohort was to the overall GUM attending population living with HIV.

At baseline (measured at the matched individual's first attendance in GUMCAD from 2009), there was evidence of statistically significant differences between the matched cohort and all men living with HIV who are captured in GUMCAD, whose baseline was measured at their first reported attendance in the GUMCAD dataset between 2009-2016. Statistically significant differences were seen in terms of age (p-value=<0.0001) and in terms of ethnicity (p-value=<0.001). This difference in sample demographics is likely to be due to 45% of MSM within the matched cohort being diagnosed with HIV prior to the start of the follow period in 2009 and missing information on an individual's HIV status in the GUMCAD dataset if previously diagnosed elsewhere.

Among the 19,428 men in the cohort, 16,441 (85.2%) were white. At the time of cohort entry, the median age was 41 (IQR:33-48), 87.4% were on ART with a median CD4 count of 530 cells/mm³ (IQR:393-700) and a median viral load of 49 copies/ml (IQR:39-216). 5,979 (33%) of men had an undetectable viral load at their first GUM attendance. Overall 82% of individuals who were not receiving ART at their first recorded visit initiated ART during the follow-up period. The median number of STI clinic attendances per year (as reported to GUMCAD) was 5 (IQR:3-9).

There were a total of 429,829 STI clinic visits during the study period, and viral load data, obtained via the matching process, were available for 87.4% of these visits (375,745/429,829), CD4 count data were available for 80.8% of visits (347,000/429,829). Where information was available, the HIV viral load was reported as virally suppressed (<50 cells/ml) in 69.3% (260,289/375,745) of visits and the CD4 count was >500 cells/mm³ in 55.8% of clinic visits.

Syphilis

Over the entire study period the rate of syphilis was 32.5 cases per 1000 person years (1000/yr) (Table 1). The rate of syphilis increased from 28.78 per 1000/yr in 2009 to 52.06 per 1000/yr in 2016 (Table 2). In univariable analysis, the rate of syphilis was highest among men aged 25-34 (41.13 per 1000/yr 95% CI:38.63-43.78 P<0.05) and 35-49 (36.84 per 1000/yr 95% CI:35.32-38.42 P<0.05) compared with those aged over 65, the age group showing the lowest risk of syphilis. The rate of syphilis was higher among men receiving ART (36.85 cases per 1000/yr 95% CI:35.56-38.20 P<0.05), compared to those not receiving ART (32.64 cases per 1000/yr 95% CI:30.25-35.21 P<0.05). Whilst this increased rate compared to men not receiving ART was significant, the absolute rate difference was only 4.21 cases per 1000/yr. Syphilis was most common among men with a high CD4 count (>500 cells per mm³) compared to those with CD4 counts

<500 cells per mm³ and among those with a viral load of <50 cells/ml compared to those with a viral load >50 cells/ml. The rate of syphilis was strongly associated with a diagnosis of other bacterial STIs during the study period. Individuals diagnosed with two or more other bacterial STIs saw a rate of syphilis of 91.31 cases per 1000/yr (95% CI:87.46-95.33 P<0.05), compared to those who were only diagnosed with one STI, with a rate of 14.53 (95% CI:13.70-15.41 P<0.05) cases per 1000/person-years.

In multivariable analysis both age and being diagnosed with other bacterial STIs remained strongly associated with the risk of syphilis. Compared to men who were not diagnosed with another STI, the risk of syphilis was significantly higher among both men with a single other bacterial STI (HR:2.93, 95% CI:2.65-3.24 P<0.05) and those diagnosed with two or more other bacterial STIs (HR:5.83, 95% CI:5.37-6.32 P<0.05). The risk of syphilis was highest among individuals aged 25-34 (HR:1.89, 95% CI:1.43-2.51 P<0.05) and 35-49 (HR:1.88, 95% CI:1.43-2.48 P<0.05). After adjustment for confounders, ART use was not significantly associated with an increased risk of syphilis (HR:1.12, 95% CI:0.99-1.27) (Table 2).

| | Episodes of infection | Years Follow-Up | Rate* (per 1000 person-years) | Upper CI (95%) | Lower CI (95%) |
|-------------------|-----------------------|-----------------|-------------------------------|----------------|----------------|
| Syphilis | 3671 | 112.96 | 32.50 | 31.46 | 33.57 |
| Chlamydia | 7606 | 112.96 | 67.33 | 65.83 | 68.86 |
| Gonorrhoea | 8814 | 112.96 | 78.02 | 76.41 | 79.67 |

Table 1. Rates of Syphilis, Chlamydia and Gonorrhoea among MSM between 2009 and 2016

*Rate represents the frequency with which an event occurs in a defined population over a specified period of time.

| | | Rate | Lower 95% CI | Upper 95%CI | Rate Ratio* | Hazard ratio | Lower 95% CI | Upper 95%CI | P value |
|---|-------------------------------|--------|--------------|-------------|-------------|--------------|--------------|-------------|---------|
| Age band | 16-24 | 27.843 | 21.793 | 35.572 | 2.078 | 1.493767 | 1.027233 | 2.172185 | 0.036 |
| | 25-34 | 41.125 | 38.632 | 43.777 | 3.069 | 1.892169 | 1.428019 | 2.507182 | 0.000 |
| | 35-49 | 36.837 | 35.317 | 38.422 | 2.749 | 1.880326 | 1.427079 | 2.477527 | 0.000 |
| | 50-64 | 24.394 | 22.585 | 26.348 | 1.82 | 1.510372 | 1.138879 | 2.003042 | 0.004 |
| | >65 (base) | 13.4 | 10.313 | 17.413 | | 1 | | | |
| ART status | On ART | 36.853 | 35.557 | 38.196 | 1.129 | 1.1203 | 0.9905048 | 1.267104 | 0.071 |
| | Not on ART (base) | 32.639 | 30.252 | 35.214 | | | | | |
| | Missing | 17.958 | 15.86 | 20.333 | 0.487 | 0.7069033 | 0.5813087 | 0.8596331 | 0.001 |
| CD4 category (cells per mm ³) | <200 | 19.376 | 15.25 | 24.618 | 0.472 | 0.809554 | 0.6281218 | 1.043393 | 0.103 |
| | 200-349 | 27.691 | 24.805 | 30.913 | 0.673 | 0.9546112 | 0.8420469 | 1.082223 | 0.468 |
| | 350-499 | 31.797 | 29.605 | 34.151 | 0.772 | 0.9004347 | 0.8246577 | 0.9831748 | 0.019 |
| | >500 (base) | 41.174 | 39.476 | 42.945 | | 1 | | | |
| | Missing | 24.971 | 23.066 | 27.033 | 0.606 | 0.8740689 | 0.7814686 | 0.9776419 | 0.018 |
| Viral Load category (copies/ml) | <50 (base) | 36.922 | 35.539 | 38.359 | | 1 | | | |
| | 50-200 | 33.658 | 28.973 | 39.101 | 0.912 | 1.019561 | 0.8682193 | 1.197283 | 0.813 |
| | >200 | 33.121 | 30.759 | 35.664 | 0.897 | 0.9980841 | 0.8836522 | 1.127335 | 0.975 |
| | Missing | 22.504 | 20.413 | 24.809 | 0.609 | 0.9437805 | 0.7986513 | 1.115282 | 0.497 |
| Other bacterial STIs | No other STIs (base) | 14.528 | 13.699 | 15.407 | | 1 | | | |
| | 1 other STI diagnosis | 44.666 | 41.541 | 48.026 | 3.074 | 2.933063 | 2.653683 | 3.241855 | 0.000 |
| | 2 or more other STI diagnoses | 91.313 | 87.463 | 95.332 | 6.285 | 5.82641 | 5.372481 | 6.318692 | 0.000 |
| Year | 2009 | 28.782 | 24.049 | 34.447 | | 1 | | | |
| | 2010 | 24.266 | 21.336 | 27.598 | 0.843 | 0.8245479 | 0.6604729 | 1.029382 | 0.088 |
| | 2011 | 28.246 | 25.314 | 31.516 | 0.981 | 0.9335637 | 0.755377 | 1.153783 | 0.525 |
| | 2012 | 24.027 | 21.526 | 26.818 | 0.835 | 0.7744598 | 0.6262373 | 0.9577646 | 0.018 |
| | 2013 | 26.59 | 24.105 | 29.331 | 0.924 | 0.8442963 | 0.686264 | 1.03872 | 0.109 |
| | 2014 | 35.883 | 33.131 | 38.865 | 1.247 | 1.129241 | 0.9244973 | 1.379329 | 0.234 |
| | 2015 | 38.078 | 35.368 | 40.995 | 1.323 | 1.20973 | 0.9919012 | 1.475397 | 0.060 |
| | 2016 | 52.06 | 48.945 | 55.374 | 1.809 | 1.748079 | 1.437501 | 2.12576 | 0.000 |

Table 2: Univariate and multivariate random-effects Poisson model analysis of Syphilis among MSM between 2009 and 2016

*Rate ratio represents the relative difference measure used to compare the incidence rates of events occurring at any given point in time.

Primary syphilis

In a sensitivity analysis including only cases of primary syphilis the risk of syphilis was not associated with ART use (HR:1.13, 95% CI:0.92-1.40). The risk of primary syphilis was strongly associated with being diagnosed with two or more other bacterial STIs (HR:5.14, 95% CI:4.49- 5.91).

Chlamydia and gonorrhoea

Over the entire study period the rate of chlamydia was 67.3 cases per 1000/yrs and gonorrhoea, 78.02 cases per 1000/yrs (Table1). Univariable analysis showed MSM not on ART had significantly higher rates of chlamydia (83.12 cases per 1000/yrs 95% CI:79.26-87.18) than those on ART (Rate ratio:0.83); gonorrhoea rates were also higher among those not on ART (100.92 cases per 1000/yrs 95% CI:96.99-105/38). When adjusting for potential confounders, the rate of chlamydia was lower among MSM on ART (HR:0.95, 95% CI:0.87-1.03), but this difference was not significant; the rate of gonorrhoea was significantly lower among MSM on ART (HR:0.93, 95% CI:0.86-1.01).

Limitations

There are several limitations in our study. Missing data on ART and HIV status at some STI attendances, may have introduced selection bias. Furthermore, the data recorded in the HIV dataset only allowed us to classify ART status as receiving or not receiving ART in a given year. We were not therefore able to explore associations between ART use and syphilis by class of ART or regimen. A methodological limitation is that ART status was carried forwards within the most recent year, therefore there is a possibility that some patients' ART status changed more frequently than was captured in our dataset. However, ART uptake is high among MSM in the UK (>95%) with high viral suppression (>95%) suggesting high adherence to ART[14], and behavioural surveys have found most people receiving ART treatment only miss one or two tablets a week[15]. We included time as a variable to account for overall secular trends, which demonstrate an overall rise in the number of cases of syphilis over the study period in the UK. Auto-correlation of time dependent variables can bias effect estimates although we note that the unadjusted rates of syphilis in individuals receiving or not receiving ART are similar suggesting this is unlikely to have significantly impacted our findings.

Additionally, although matching between the HIV and STI datasets was generally good, differences between the HIV and STI surveillance variables meant that there were limitations to the matching processes. The representativeness of this sample is difficult to assess, therefore extrapolation of our findings to all MSM living with HIV should be done with caution. Finally, we could not measure high-risk sexual behaviour directly and instead generated a behavioural proxy based on other bacterial STI coinfections. This approach has previously been validated [16], however, people are likely to go in and out of high risk periods and it is likely we have overestimated periods of high-risk which would potentially underestimate their effect in our model[13].

Additionally, any associations between ART and syphilis may be confounded by secular trends; we noted marked increases in the rates of syphilis, chlamydia and gonorrhoea in the period 2009-2016 suggesting broader secular trends in sexual networking and risk-taking may explain increases in syphilis during the study period. This temporal increase may confound the association between ART and syphilis, as the introduction of revised ART guidelines in the UK in 2011 [17] led to a greater proportion of people living with HIV starting ART in more recent years.

Discussion

Using nationally comprehensive data on MSM living with HIV, we found a higher incidence of syphilis among those on ART compared to those not on ART, an association that was not found with chlamydia or gonorrhoea. However, after adjusting for confounders, there was no evidence of a statistically significant association between syphilis and ART. The higher incidence of syphilis in MSM on ART is therefore likely driven by higher risk behaviours, as evidenced by the increased risk found in men meeting our proxy measure for high-risk (at least 2 other STIs).

Although no significant association is seen, the results show higher rates of syphilis among virally suppressed individuals (<50 copies/ml) and those with a high CD4 count (>500 cells per mm³). This may suggest some indirect association between the use of ART and syphilis incidence. However, our findings do not provide evidence to support the hypothesis postulated by Rekart and colleagues that an increased risk of syphilis seen among MSM is due to a direct action of ART, nor that increased ART rollout can directly explain the recent significant increase in the number of syphilis cases seen in England.

The lack of association between syphilis and ART is also in keeping with studies of STI rates among people receiving pre-exposure prophylaxis for HIV (PrEP). Studies have reported varying impacts on the risk of bacterial STIs among individuals receiving PrEP. Whilst there is some evidence the rate of bacterial STIs is increased among individuals receiving PrEP, likely reflecting behavioural changes and increases in STI testing frequency, there is no evidence of a disproportionate change in the risk of syphilis[18-20].

Despite its limitations, this analysis was performed using one of the most comprehensive national HIV cohorts, including clinical data on persons accessing HIV care and STI diagnoses captured through a national prospective dataset using standardised criteria. To our knowledge, this is the largest study ever conducted to assess the association between ART use and the risk of syphilis. Despite finding no clear evidence of a link between ART and syphilis, our results do highlight considerable increases in the rates of syphilis in MSM living with HIV over the study period 2009 to 2016. Further investigation using more robust behavioural data is needed to investigate into the potential reasons for this increase are needed to provide improvements in the prioritisation of the screening, diagnosis and treatment of STIs in MSM. Improved strategies to target these particularly high risk sexual networks are needed to reduce the incidence of bacterial STIs among high risk men.

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Contributorship statement

Hester Allen carried out the analysis and write up of this project. Peter Kirwan designed and executed the data matching between STI and HIV datasets. Alison Brown, Hamish Mohammed and Gwenda Hughes helped to supervise the project and provided statistical and interpretive guidance. Michael Marks and Valerie Delpech designed the project and provided supervision and provided major interpretive guidance.

1. Hughes, G. and N. Field, *The epidemiology of sexually transmitted infections in the UK: impact of behavior, services and interventions*. Future Microbiol, 2015. **10**(1): p. 35-51.
2. Public Health England, *Sexually transmitted infections and screening for chlamydia in England, 2018: Health Protection Report*. 2019.
3. Shilaih, M., et al., *Factors associated with syphilis incidence in the HIV-infected in the era of highly active antiretrovirals*. Medicine (Baltimore), 2017. **96**(2): p. e5849.
4. Golden, M.R., et al., *HIV serosorting in men who have sex with men: is it safe?* J Acquir Immune Defic Syndr, 2008. **49**(2): p. 212-8.
5. Public Health England, *Substance misuse services for men who have sex with men involved in chemsex*. 2015.
6. Mohammed, H., et al., *Increase in Sexually Transmitted Infections among Men Who Have Sex with Men, England, 2014*. Emerging infectious diseases, 2016. **22**(1): p. 88-91.
7. British Association for Sexual Health and HIV, *Standards for the management of sexually transmitted infections (STIs) in outreach services*. . 2016.
8. Rekart, M.L., et al., *A double-edged sword: does highly active antiretroviral therapy contribute to syphilis incidence by impairing immunity to Treponema pallidum?* Sexually transmitted infections, 2017. **93**(5): p. 374-378.
9. England, P.H. *HIV surveillance systems*. 2008 01/09/2019]; Available from: <https://www.gov.uk/guidance/hiv-surveillance-systems>.
10. GOV.UK. *GUMCAD STI Surveillance System*. 2019; Available from: <https://www.gov.uk/guidance/gumcad-sti-surveillance-system>.
11. Savage, E.J., et al., *Improving surveillance of sexually transmitted infections using mandatory electronic clinical reporting: the genitourinary medicine clinic activity dataset, England, 2009 to 2013*. Euro Surveill, 2014. **19**(48): p. 20981.
12. Winter, J.R., et al., *Trends in, and factors associated with, HIV infection amongst tuberculosis patients in the era of anti-retroviral therapy: a retrospective study in England, Wales and Northern Ireland*. BMC medicine, 2018. **16**(1): p. 85-85.
13. Desai, S., et al., *HIV incidence in an open national cohort of men who have sex with men attending sexually transmitted infection clinics in England*. HIV Med, 2017. **18**(9): p. 615-622.
14. Brown, A.E., et al., *Towards elimination of HIV transmission, AIDS and HIV-related deaths in the UK*. HIV Med, 2018.
15. England, P.H. *Positive Voices : National Survey of People Living with HIV 2017*; Available from: <https://www.ucl.ac.uk/voices>.
16. Furegato, M., et al., *The role of frequent HIV testing in diagnosing HIV in men who have sex with men*. HIV Med, 2018. **19**(2): p. 118-122.
17. Nelson, M., et al., *British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011*. HIV Med, 2011. **12 Suppl 2**: p. 1-140.
18. Volk, J.E., et al., *No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting*. Clin Infect Dis, 2015. **61**(10): p. 1601-3.
19. Traeger, M.W., et al., *Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection*. Jama, 2019. **321**(14): p. 1380-1390.
20. Traeger, M.W., et al., *Effects of Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection on Sexual Risk Behavior in Men Who Have Sex With Men: A Systematic Review and Meta-analysis*. Clin Infect Dis, 2018. **67**(5): p. 676-686.

